After entry of this amendment, claims 1, 3-6 and 10 are pending in this application. Consideration of these claims is requested.

Claim objections:

Claim 10 was objected to as being drawn to a non-elected invention. As suggested by the Examiner, claim 10 has been amended to make it dependent on claim 1 and to provide antecedent basis for the term "composition," while keeping the claim scope within elected Group I. Applicants request that this claim objection be withdrawn.

Claim rejections under 35 U.S.C. §112, first paragraph:

Claims 1-6 and 10 are rejected under 35 U.S.C. §112, first paragraph, for allegedly failing to enable one of skill in the art to make or use the invention commensurate in scope with the claims. Applicants respectfully disagree. However, to advance prosecution of this case, applicants have amended the claims and request reconsideration of these claims in light of the amendments and the arguments presented herein.

Applicants demonstrate throughout the specification that a recombinant protein may be constructed comprising epitopes from two or more stages in a life cycle of *Plasmodium falciparum* (see *e.g.*, Example 1 and specification page 9, line 6 through page 11, line 15). Furthermore, the amendments to the claims made herein specify that the epitopes of the recombinant protein comprise SEQ ID NO: 3-25. Hence, applicants submit that the amended claims submitted herewith are amply supported by the specification, which clearly teaches one of ordinary skill in the art how to make and use the claimed recombinant protein. Applicants request that the rejections under 35 U.S.C. § 112 be withdrawn.

Claim rejections under 35 U.S.C. §102:

Gilbert *et al.*

Claims 1-3, 5, 6 and 10 are rejected under 35 U.S.C. §102, as allegedly being anticipated by Gilbert *et al. Nature Biotechnology* 15: 1280-1284, November 1997. The Office action alleges that Gilbert *et al.*, teach a recombinant protein comprising antigenic epitopes of *Plasmodium falciparum* that appears to be the same as the claimed invention. Applicants submit

herewith evidence in the form of a Declaration under 37 C.F.R. § 131 of Dr. Ya Ping Shi to overcome Gilbert *et al.* The Declaration and Exhibits A and B, submitted in support of the Declaration, provide evidence that the inventors of the current application reduced the invention that is the subject matter of the current application to practice prior to November 1997, the effective date of Gilbert *et al.* The exact dates have been redacted, but are prior to the effective date of Gilbert *et al.*, November 1997.

The recombinant protein claimed herein, synthetic vaccine antigen construct CDC/NIMALVAC-1, is composed of twelve B-cell and nine T-cell epitopes derived from nine stage-specific vaccine candidate antigens of *P. falciparum* (see specification pg. 10, lines 23-25 and Table 1). In her Declaration, Dr. Shi states that she synthesized CDC/NIMALVAC-1 prior to November 1997. Exhibit B is a record from the CDC Biotechnology Core Facility, providing evidence of Dr. Shi's request for synthesis of several oligonucleotides. These oligonucleotides were used as forward and reverse complementary primers for the Polymerase Chain Reaction (PCR) amplification of CDC/NIMALVAC-1, as is depicted in Figure 2 of the specification.

In addition, Exhibit A consists of photocopies of several pages from Dr. Shi's laboratory notebook. The experiments noted on these pages (discussed in detail in the Declaration) show the strategy for synthesis of CDC/NIMALVAC-1, and results confirming that CDC/NIMALVAC-1 was successfully constructed. Included in the laboratory notebook pages are calculations for PCR reactions for amplification of segments using the above-referenced oligonucleotides to generate a final amplification product, restriction endonuclease reactions to cleave the amplification product at specific locations, and ligation reactions to clone the amplification product into an expression vector for expression as a recombinant protein. Also referenced in the Declaration are the sequencing experiments performed by Dr. Shi to confirm that the sequence of the clone was correct on the molecular level.

As is stated in the Declaration, the sequencing experiments indicated that one error existed in each of clones 20 and 63. Thus, Dr. Shi constructed the final sequence, CDC/NIMALVAC-1, using methylation to block restriction endonuclease sites on the vector and cloning the correct segments of clone 20 and 63 into the final construct, clones 31A and 31B, which are both duplicates of CDC/NIMALVAC-1.

Applicants submit that the data set forth in Exhibits A and B, in conjunction with the Declaration submitted under 37 C.F.R § 131, provide ample evidence that the inventors of the current application reduced the invention that is the subject matter of the claims of the current application to practice prior to November 1997, the effective date of Gilbert *et al.* Hence, applicants have complied with the requirements of MPEP § 715 to overcome Gilbert *et al.*, and request that the rejection of claims 1-3, 5, 6 and 10, based upon this reference, be withdrawn.

Shi *et al.*

Claims 1-3, 5, 6 and 10 are rejected under 35 U.S.C. § 102(a) as allegedly being anticipated by Shi *et al.*, *Proc. Natl. Acad. Sci., U.S.A.*, 96(4): 1615-1620. This publication is the inventors' own work.

Applicants submit herein, as Exhibit C, a copy of the Corrected Filing Receipt as mailed by the U.S. Patent Office on May 7, 2002, which demonstrates that this application claims the benefit of U.S. Provisional Application No 60/097,703, filed August 21, 1998. As the priority date of the current application is August 21, 1998, which is prior to the reference cited by the Office action, applicants point out that Shi *et al.* is not available as a reference for citation against the claims of the current application and request that the rejection of claims 1-3, 5, 6 and 10, based upon this reference, be withdrawn.

Claim rejections under 35 U.S.C. §103:

Claim 4 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Shi *et al.*, or Gilbert *et al.*, in view of Schmitt *et al.*, *Molecular Biology Reports*, 18: 223-230, 1993. As discussed above, a rejection based on Gilbert *et al.* should not be sustained in view of the Declaration submitted herein, which shows that the inventors of the current application reduced the invention that is the subject matter of the claims of the current application to practice prior to the effective date of Gilbert *et al.* Similarly, a rejection based on Shi *et al.* should not be sustained in view of the copy of the Corrected Filing Receipt submitted herein, which demonstrates that the priority date of the current application is prior to the publication date of Shi *et al.*

Schmitt *et al.* teach affinity purification of using histidine-tagged recombinant proteins, but do not teach a recombinant protein comprising antigenic epitopes of *Plasmodium falciparum* as disclosed in the current application. Therefore, applicants submit that Schmitt *et al.* does not render the claims of the current application obvious and request that the rejection based upon this reference be withdrawn.

Other prior art cited, but not relied upon:

Applicants acknowledge that the Examiner considers Szarfman *et al.*, *Parasite Immunol.*, 10(3): 339-351,1988 and Patarroyo *et al.*, *Nature*, 328(6131):629-632, 1997 to be cited prior art.

CONCLUSIONS

It is respectfully submitted that the present claims are in condition for allowance. If it may further issuance of these claims, the Examiner is invited to call the undersigned patent attorney at the telephone number listed below.

Respectfully submitted,

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Marked-up Version of Amended Claims
Pursuant to 37 C.F.R. §§ 1.121(b)-(c)

1. (amended) A recombinant protein comprising peptides from two or more stages in a life cycle of *Plasmodium falciparum*, wherein each peptide comprises an antigenic epitope comprising the amino acid sequence as set forth as SEQ ID NOs: 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25.

Please cancel claim 2.

3. (amended) The protein of claim 1, comprising the amino acid sequence of SEQ ID NO: 2~~, fragments thereof, or conservative substitutions thereof that maintain antigenicity~~.

4. (reiterated) The protein of claim 1, further comprising a signal peptide polyhistidine, and a T-cell helper epitope.

5. (amended) The protein of claim 1, wherein the stages are ~~selected from the group consisting of~~ one or more of sporozoite stage, liver stage, blood stage ~~and~~ or sexual stage.

6. (reiterated) The protein of claim 5, comprising at least one antigenic epitope from each of the sporozoite, liver, blood, and sexual stages of *Plasmodium falciparum* life cycle.

Please cancel claims 7-9.

10. (amended) ~~The~~ A protein composition comprising the recombinant protein of claim ~~7~~1, in a pharmaceutically acceptable carrier.

Please cancel claims 11-12.